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PATENT
Attorney Docket No.: 16528A-000461US
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

William J. Dower, et al.

Application No.: Unassigned
Parent Application No.: 09/261,731

Filed: Herewith
Parent Filed: March 3, 1999

For: PEPTIDE LIBRARY AND
SCREENING SYSTEMS

Examiner: Unassigned
Parent Examiner: H. Park

Art Unit: Unassigned
Parent Art Unit: 1645

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to calculating the claims fee, please enter the following amendments in the above-identified application.

IN THE SPECIFICATION

Kindly amend the specification as follows:

At page 1, line 6, please add --Cross-References to Related Applications--.

At page 1, line 7, please add -- This application is a continuation of U.S. Patent Application No. 09/261,731, filed March 3, 1999; which is a continuation of U.S. Patent Application No. 08/914,403, filed August 19, 1997; which is a continuation of U.S. Patent Application No. 07/541,108, filed June 20, 1990 and issued as U.S. Patent No. 5,723,286.

Each of the foregoing priority applications, inclusive of the disclosure, claims and amendments presented therein, is incorporated by reference herein in their entirety. --

IN THE CLAIMS:

Please cancel claims 1-32, without prejudice.

Please add new claims 33-73 as follows:

- 1 --33. A method of identifying a peptide, polypeptide or protein having a
2 binding property to a ligand, comprising:
 - 3 (a) providing a ligand for detecting said binding property;
 - 4 (b) synthesizing a diverse population of randomly generated
5 polynucleotide sequences;
 - 6 (c) inserting said diverse population of randomly generated
7 polynucleotide sequences into a population of expression vectors to form a diverse population
8 of expression vectors containing randomly generated polynucleotide sequences;
 - 9 (d) expressing in host cells said diverse population of expression
10 vectors containing randomly generated polynucleotide sequences to produce a diverse
11 population of peptides, polypeptides or proteins; and
 - 12 (e) screening said diverse population of peptides, polypeptides or
13 proteins with said ligand under conditions which allow binding and detection of one or more
14 peptides, polypeptides or proteins having said predetermined property.
- 1 34. An isolated, diverse population of peptides, polypeptides, or proteins
2 comprising greater than about 1×10^5 different random amino acid sequences encoded by
3 random polynucleotide sequences.
- 1 35. A method of isolating a polynucleotide sequence encoding a peptide,
2 polypeptide or protein having a predetermined binding property to a ligand, comprising:
 - 3 (a) providing a ligand for detecting said binding property;
 - 4 (b) synthesizing a diverse population of randomly generated
5 polynucleotide sequences;

6 (c) inserting said diverse population of randomly generated
7 polynucleotide sequences into a population of expression vectors to form a diverse population
8 of expression vectors containing randomly generated polynucleotide sequences;

9 (d) expressing in host cells said diverse population of expression
10 vectors containing randomly generated polynucleotide sequences to produce a diverse
11 population of peptides, polypeptides or proteins;

12 (e) screening said diverse population of peptides, polypeptides or
13 proteins with said ligand under conditions which allow binding and detection of one or more
14 peptides, polypeptides or proteins to said ligand; and

15 (f) isolating the randomly generated polynucleotide sequence or
16 sequences which encoding said peptides, polypeptides or proteins having said predetermined
17 binding property to said ligand.

1 36. An isolated, diverse population of polynucleotide sequences which
2 encode a diverse population of ligand binding peptides, polypeptides, or proteins comprising
3 greater than about 1×10^5 different random amino acid sequences encoded by the random
4 polynucleotide sequences.

1 37. A method of isolating a peptide, polypeptide or protein having a binding
2 property, comprising:

3 (a) providing a ligand for detecting said binding property;

4 (b) synthesizing a diverse population of randomly generated
5 polynucleotide sequences;

6 (c) inserting said diverse population of randomly generated
7 polynucleotide sequences into a population of expression vectors to form a diverse population
8 of expression vectors containing randomly generated polynucleotide sequences;

9 (d) expressing in host cells said diverse population of expression
10 vectors containing randomly generated polynucleotide sequences to produce a diverse
11 population of peptides, polypeptides or proteins;

(e) screening said diverse population of peptides, polypeptides or proteins with said ligand under conditions which allow binding and detection of one or more peptides, polypeptides or proteins having said predetermined property;

(f) isolating the randomly generated polynucleotide sequence or sequences encoding said peptides, polypeptides or proteins having said binding property to said ligand; and

(g) using genetic information from said isolated randomly generated polynucleotide sequence to produce said peptide, polypeptide or protein having said binding property.

38. A method of producing a diverse population of randomly generated polynucleotide sequences encoding a diverse population of ligand binding peptides, polypeptides or proteins, comprising:

(a) synthesizing a diverse population of randomly generated polynucleotide sequences selected from a method consisting of random copolymerization of double stranded oligonucleotides, copolymerization of the four kinds of nucleotide triphosphates consisting of Adenine, Cytosine, Guanine and Thymine, and chemical synthesis; and

(b) inserting said diverse population of randomly generated polynucleotide sequences into a population of vectors to form a diverse population of vectors containing randomly generated polynucleotide sequences.

39. An isolated, diverse population of vectors comprising randomly generated polynucleotide sequences encoding a diverse population of ligand binding peptides, polypeptides, or proteins comprising greater than about 1×10^5 different random amino acid sequences.

40. An isolated, diverse population of peptides or polypeptides comprising random amino acid sequences encoded by random polynucleotide sequences of about 300 nucleotides or less in length.

43. An isolated, diverse population of peptides, polypeptides, or proteins comprising random amino acid sequences produced by a method comprising synthesizing a diverse population of randomly generated polynucleotide sequences selected from a method consisting of random copolymerization of double stranded oligonucleotides, copolymerization of the four kinds of nucleotide triphosphates consisting of Adenine, Cytosine, Guanine and Thymine, and chemical synthesis; and expressing said randomly generated polynucleotide sequences.

producing by enzymatic or chemical coupling, stochastically generated polynucleotide sequences;

culturing host cells containing the vectors to produce peptides, polypeptides, or proteins encoded by the stochastically generated polynucleotide sequences;

isolating a stochastically generated polynucleotide sequence which encodes the identified peptide, polypeptide, or protein;

using the isolated sequence to produce the peptide, polypeptide, or protein having the predetermined property.

1 45. A process for the production of a transcription product or a translation
2 product, comprising the steps of:
3 producing a stochastically-generated polynucleotide sequence;
4 producing a library of expression vectors comprising said stochastic
5 polynucleotide sequence;
6 transforming or transfecting a competent host cell clone with said library
7 of expression vectors;
8 amplifying said transformed or transfected competent clone;
9 screening and/or selecting said transformed or transfected clone in order
10 to isolate a clone expressing a stochastic polynucleotide sequence capable of synthesizing a
11 transcription product or a translation product having a predetermined property; and
12 isolating said selected or screened transformed clone;
13 isolating a stochastically generated polynucleotide sequence which
14 encodes the identified transcription product or translation product
15 using the isolated sequence to produce the transcription product or
16 translation product having the predetermined property.

1 46. A process for the production of a transcription product or a translation
2 product, comprising the steps of:
3 producing a diverse population of stochastic polynucleotide sequences;
4 inserting said stochastic polynucleotide sequences into expression
5 vectors to form a diverse population of expression vectors;
6 transforming or transfecting competent host cell clones with said diverse
7 population of expression vectors comprising said stochastic polynucleotide sequences;
8 amplifying said transformed or transfected competent clone;
9 screening and/or selecting said transformed or transfected clones in
10 order to isolate a clone expressing a stochastic polynucleotide capable of synthesizing a
11 transcription product or a translation product having the predetermined property;
12 isolating said selected or screened transformed clone;

13 isolating said stochastic polynucleotide sequence which encodes the
14 identified transcription product or translation product;
15 using the isolated stochastic polynucleotide sequence so as to produce
16 the transcription product of translation product having the predetermined property.

47. A process for the production of a polynucleotide comprising,
producing in an appropriate buffer a diverse population of stochastic
polynucleotide sequences;
inserting said stochastic polynucleotide sequences into vectors to form a
diverse population of vectors;
introducing said diverse population of vectors into host cells in a manner
to produce a diverse population of transformed host cells;
producing independent clones of the host cells so produced;
screening and/or selecting said independent clones of the host cells to
identify host cells comprising a stochastic polynucleotide sequence having at least one desired
property; and
isolating said stochastic polynucleotide sequence from the selected or
screened clones of host cells.

48. A process for the production of an RNA comprising,
producing in an appropriate buffer a diverse population of stochastic
polynucleotide sequences;
inserting said stochastic polynucleotide sequences into vectors to form a
diverse population of vectors;
introducing said diverse population of vectors into host cells in a manner
to produce a diverse population of transformed host cells;
producing independent clones of transformed or transfected host cells;
screening and/or selecting said independent clones of the host cells to
identify host cells comprising a stochastic polynucleotide sequence capable of producing RNA
having at least one desired property; and

isolating said stochastic polynucleotide sequence from the selected or screened clones of host cells.

49. A library of vectors produced by the process of claim 45 wherein said library comprises stochastic nucleotide sequences encoding for at least 10,000 transcription products or translation products.

50. A method of identifying a polynucleotide having a predetermined property, comprising:

(a) producing a population of polynucleotides comprising greater than about 1×10^5 different stochastic polynucleotide sequences;

(b) screening said population of polynucleotides for said predetermined property under conditions which allow detection of one or more polynucleotides having said predetermined property.

51. A method of identifying a polynucleotide having a binding property to a ligand, comprising:

(a) synthesizing a population of stochastic polynucleotide sequences;

(b) inserting said population of stochastic polynucleotide sequences into a population of vectors to form a population of vectors containing stochastic polynucleotide sequences;

(c) expressing in host cells said population of vectors containing stochastic polynucleotide sequences to produce a diverse population of expressed polynucleotides, and

(d) screening said diverse population of polynucleotides with a ligand under conditions which allow binding and detection one or more polynucleotides having said binding property to said ligand.

52. A method of isolating a polynucleotide having a predetermined property, comprising:

3 (a) producing a population of polynucleotides comprising greater
4 than 1×10^5 different stochastic polynucleotide sequences;

5 (b) screening said population of stochastic polynucleotide sequences
6 for said predetermined property under conditions which allow detection of one or more
7 polynucleotides having said predetermined property, and

8 (c) isolating the one or more polynucleotide sequences having said
9 predetermined property.

1 53. A method of isolating a polynucleotide having a binding property to a
2 ligand, comprising:

3 (a) synthesizing a population of stochastic polynucleotide
4 sequences;

5 (b) inserting said population of stochastic polynucleotide sequences
6 into a population of vectors to form a population of vectors containing stochastic
7 polynucleotide sequences;

8 (c) expressing in host cells said population of vectors containing
9 stochastic polynucleotide sequences to produce a diverse population of expressed
10 polynucleotides, and

11 (d) screening said diverse population of polynucleotides with a
12 ligand under conditions which allow binding and detection of one or more polynucleotides to
13 said ligand, and

14 (e) isolating the stochastic polynucleotide sequence or sequences
15 having said binding property to said ligand.

1 54. A method of producing a diverse population of polynucleotides,
2 comprising stochastically copolymerizing a population of polynucleotides so as to produce a
3 new population of polynucleotides containing greater than about 1×10^6 different
4 polynucleotide sequences.

1 55. A method of producing a diverse population of polynucleotides,
2 comprising:

3 (a) obtaining one or more populations of polynucleotides;
4 (b) cleaving the one or more populations of polynucleotides, and
5 (c) stochastically copolymerizing the one or more populations of
6 cleaved polynucleotides so as to produce a new population of greater than about 1×10^5
7 different polynucleotide sequences.

1 56. An isolated population of polynucleotides, comprising greater than
2 about 1×10^5 different stochastic polynucleotide sequences.

1 57. A process for the production of a peptide, polypeptide, or protein having
2 a predetermined property, comprising the steps of:

3 producing by synthetic polynucleotide coupling, a population of
4 randomly generated polynucleotide sequences;

5 forming a library of expression vectors containing said population of
6 randomly generated polynucleotide sequences;

7 introducing the vectors into host cells;

8 culturing the host cells;

9 carrying out screening or selection on said host cells, to identify a
10 peptide, polypeptide, or protein produced by the host cells having the predetermined property;

11 isolating a randomly generated polynucleotide sequence which encodes
12 the identified peptide, polypeptide, or protein;

13 using the isolated sequence to produce the peptide, polypeptide, or
14 protein having the predetermined property.

1 58. A process for the production of a peptide, polypeptide, or protein having
2 a predetermined property, comprising the steps of:

3 producing a population of at least partially random synthetic
4 polynucleotide sequences;

5 introducing the population of at least partially random polynucleotide
6 sequences into host cells to produce transformed host cells;

7 cultivating the transformed host cells to produce peptides, polypeptides,
8 or proteins expressed by at least some of the random polynucleotide sequences;
9 carrying out screening and/or selection methods on said transformed
10 host cells to identify clones producing the peptide, polypeptide, or protein having the
11 predetermined property;
12 isolating the clones so identified; and
13 growing the isolated clones in a manner so as to produce the peptide,
14 polypeptide, or protein having the predetermined property.

1 59. A process for the detection or titration of a ligand using a peptide,
2 polypeptide, or protein having a predetermined property, comprising the steps of:
3 producing by synthetic polynucleotide coupling, a population of
4 randomly generated polynucleotide sequences;
5 forming a library of expression vectors containing said population of
6 randomly generated polynucleotide sequences;
7 introducing the vectors into host cells;
8 culturing the host cells containing the vectors to produce peptides,
9 polypeptides, or proteins encoded by the randomly generated polynucleotide sequences;
10 carrying out screening or selection on said host cells, to identify a
11 peptide, polypeptide, or protein produced by the host cells having the predetermined property;
12 contacting the peptide, polypeptide, or protein with two or more
13 concentrations of a ligand; and
14 determining the amount of peptide, polypeptide or protein bound at each
15 concentration of ligand.

1 60. A process for the detection or titration of a ligand using a peptide,
2 polypeptide, or protein having a predetermined property, comprising the steps of:
3 producing a population of at least partially random synthetic
4 polynucleotide sequences;
5 introducing the population of at least partially random polynucleotide
6 sequences into host cells to produce transformed host cells;

7 cultivating the transformed host cells to produce peptides, polypeptides,
8 or proteins expressed by at least some of the random polynucleotide sequences;
9 carrying out screening and/or selection methods on said transformed
10 host cells to identify clones producing the peptide, polypeptide, or protein having the
11 predetermined property;
12 contacting the peptide, polypeptide, or protein with two or more
13 concentrations of a ligand; and
14 determining the amount of peptide, polypeptide or protein bound at each
15 concentration of ligand.

1 61. A method of identifying a peptide, polypeptide or protein having a
2 predetermined property, comprising:

- 3 (a) producing a population of peptides, polypeptides or proteins
4 encoded by random polynucleotide sequences;
5 (b) screening said population of peptides, polypeptides or proteins
6 for said predetermined property under conditions which allow detection of one or more
7 peptides, polypeptides or proteins having said predetermined property.

1 62. A method of producing a peptide, polypeptide or protein having a
2 predetermined property, comprising:

- 3 (a) producing a population of peptides, polypeptides or proteins
4 encoded by random polynucleotide sequences;
5 (b) screening said population of peptides, polypeptides or proteins
6 for said predetermined property under conditions which allow detection of one or more
7 peptides, polypeptides or proteins having said predetermined property;
8 (c) isolating the polynucleotide sequence encoding said one or more
9 peptides, polypeptides or proteins having said predetermined property; and
10 (d) producing said peptide polypeptide or protein.

1 63. A method of producing a random polynucleotide population, comprising
2 synthesizing random polynucleotide sequences.

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1 64. A method of producing a desired compound, comprising combining a
2 population of peptides, polypeptides or proteins encoded by random polynucleotide sequences
3 with two or more reactant precursors under conditions favorable for said precursors to react,
4 and incubating said population of peptides, polypeptides or proteins with said reactant
5 precursors for sufficient time so as to allow the catalysis of said desired compound.

1 65. A method of identifying a population of peptides, polypeptides or
2 proteins which catalyze a sequence of chemical reactions, comprising:

3 (a) combining a population of peptides, polypeptides or proteins
4 encoded by random polynucleotide sequences with two or more reactant precursors under
5 conditions favorable for said precursors to react;

6 (b) incubating said population of peptides, polypeptides or proteins
7 with said reactant precursors for sufficient time to allow the catalysis of said sequence of
8 chemical reactions, and

9 (c) determining the presence or absence of a compound produced by
10 said sequence of chemical reactions, the presence of said compound indicating that said
11 population of peptides, polypeptides or proteins can catalyze said sequence of chemical
12 reactions.

1 66. A process for the production of an expression vector which comprises at
2 least one random sequence of polynucleotides, comprising the steps of:

3 providing in an appropriate buffer at least three different sequences of
4 oligonucleotides, said oligonucleotides each comprising at least 7 nucleotide residues;

5 polymerizing said oligonucleotides to form a random sequence of
6 polynucleotides; and

7 ligating said random sequence of polynucleotides into a linearized
8 expression vector.

1 67. A process for the production of an expression vector capable of
2 producing a transcription product or a translation product comprising at least one random
3 sequence of polynucleotides, comprising the steps of:

4 linearizing an expression vector;
5 reacting said linearized expression vector with terminal transferase
6 enzyme in the presence of desired ratios of deoxynucleotide- triphosphates of guanine,
7 cytosine, thymidine, and adenine to form a random polynucleotide sequence at each 3'
8 extremity of said linearized vector;
9 hybridizing said random polynucleotide sequence at a 3' extremity of
10 said linearized vector; and
11 synthesizing a second strand from said 3' ends of said hybridized vector
12 by incubating with polymerase.

1 68. A process for the production of a library of expression vectors capable
2 of producing a transcription product or a translation product, said vectors comprising at least
3 one random sequence of polynucleotides, comprising the steps of:
4 producing at least one random sequence of polynucleotides;
5 ligating said random sequence of polynucleotides into an expression
6 vector;
7 transforming a competent clone with said ligated expression vector;
8 culturing said transformed clone;
9 screening and/or selecting said transformed clone in order to isolate a
10 clone expressing a random polynucleotide leading to the synthesis of a transcription product or
11 a translation product;
12 isolating said selected or screened transformed clone; and
13 isolating the expression vector cultured in said selected or screened
14 transformed clone so identified.

1 69. A library of expression vectors capable of producing a transcription
2 product or a translation product, said expression vectors comprising at least one random
3 sequence of polynucleotides, produced in accordance with the process of claim 67.

1 70. An expression vector produced in accordance with the process of claim
2 66, 67, or 68.

1 71. A method of producing a diverse population of vectors comprising:
2 (a) synthesizing a diverse population of randomly generated
3 polynucleotide sequences comprising greater than about 1×10^5 different polynucleotide
4 sequences, said method consisting of random copolymerization of double stranded
5 oligonucleotides, copolymerization of the four kinds of nucleotide triphosphates consisting of
6 adenine, cytosine, guanine and thymine, and chemical synthesis, and

7 (b) inserting said diverse population of randomly generated
8 polynucleotide sequences into a population of vectors to form a diverse population of vectors
9 containing randomly generated polynucleotide sequences.

1 72. A method of producing a diverse population of vectors, comprising
2 randomly copolymerizing a diverse population of vectors containing double stranded
3 polynucleotides so as to produce a new population of vectors containing greater than about
4 1×10^5 different polynucleotide sequences.

1 73. A method of producing a diverse populations of vectors, comprising:
2 (a) obtaining one or more diverse populations of vectors containing
3 diverse sequences of double stranded polynucleotides;
4 (b) digesting the one or more diverse populations of vectors with a
5 restriction enzyme, and
6 (c) randomly copolymerizing the one or more diverse populations of
7 double stranded polynucleotides so as to produce a new population of greater than about 1×10^5
8 different polynucleotide sequences.--

REMARKS

With entry of this amendment, claims 33-73 are pending in the application. By this amendment, claims 1-32 have been canceled without prejudice and with reservation of all rights to pursue the subject matter of these claims in one or more related applications.

The present continuation application, inclusive of this Preliminary Amendment, carries forward aspects of the invention presented in the parent application, U.S. Patent

Application No. 09/261,731, filed March 3, 1999, which is incorporated in the present application in its entirety inclusive of the amendments presented therein. In particular, the present amendment carries forward aspects of the invention presented in the First Preliminary Amendment, filed in the parent application on March 3, 1999, the Second Preliminary Amendment, filed June 9, 1999, the Third Preliminary Amendment, filed September 29, 1999, the Fourth Preliminary Amendment, filed October 6, 1999, and the Fifth Preliminary Amendment filed October 20, 1999. Collectively, the claims originally presented by these serial amendments in the parent case were directed to subject matter that corresponds to, or substantially corresponds to, comprehensively, the subject matter claimed in the following patents issued to Kauffman and Ballivet: U.S. Patent No. 5,723,323, issued March 3, 1998, U.S. Patent No. 5,763,192, issued June 9, 1998; U.S. Patent No. 5,814,476, issued September 29, 1998; U.S. Patent No. 5,817,483, issued October 6, 1998; and U.S. Patent No. 5,824,514, issued October 20, 1998 (copies of each these patents were presented in the parent application and are incorporated herein). As noted in the parent case, these claims were presented in a timely fashion to preserve Applicant's rights pursuant to 35 U.S.C. §135(b).

For this same purpose, the present application and Preliminary Amendment are submitted to focus examination on generic aspects of the invention presented in the parent case and corresponding to generic aspects of the subject matter claimed in the above-identified series of patents issued to Kaufmann and Ballivet. To facilitate examination of these generic aspects of Applicants' invention, the present application carries forward only the independent claims presented in the parent application, that read on generic subject matter claimed in the foregoing Kaufmann and Ballivet patents. Thus, claims 33-43 are presented by this amendment and are believed to correspond identically to, or to correspond substantially to, claims 1, 15, 16, 24, 25, 34, and 41-45, respectively, of U.S. Patent No. **5,723,323**, issued to Kauffman and Ballivet on March 3, 1998. These claims carry forward directly the subject matter of independent claims 33, 45, 46, 54, 55, 64, 71, 72, 73, 74, and 75 presented in the First Preliminary Amendment filed with the parent application on March 3, 1999. Claim 44 presented by this amendment are believed to correspond identically to, or to correspond substantially to claim 1, of U.S. Patent No. **5,763,192**, issued June 9, 1998. This claim carries forward directly the subject matter of independent claim 79 presented in the Second

Preliminary Amendment filed in the parent application on June 9, 1999. Claims 45-56 presented by this amendment are believed to correspond identically to, or to correspond substantially to, claims 1-3, 8, 14, 15, 29, 47, 61, 79, 91 and 103, respectively, of U.S. Patent No. **5,814,476**, issued September 29, 1998. These claims carry forward directly the subject matter of independent claims 83, 84, 85, 90, 96, 97, 111, 129, 143, 161, 173, and 185 presented in the Third Preliminary Amendment filed in the parent application on September 29, 1999. Claims 57-65 presented by this amendment are believed to correspond identically to, or to correspond substantially to, claims 1-4, 6, 17, 29, 35 and 36, respectively, of U.S. Patent No. **5,817,483**, issued October 6, 1998. These claims carry forward directly the subject matter of independent claims 190, 191, 192, 193, 195, 206, 218, 224, and 225 presented in the Fourth Preliminary Amendment filed in the parent application on October 6, 1999. Claims 66-73 presented by this amendment and are believed to correspond identically to, or to correspond substantially to claims 1, 11, 12, 13, 14, 18, 27, and 37, respectively, of U.S. Patent No. **5,824,514**, issued October 20, 1998. These claims carry forward directly the subject matter of independent claims 243, 253, 254, 255, 256, 260, 269, and 279 presented in Fifth Preliminary Amendment filed in the parent application on October 20, 1999.

The claims presented herein are intended to fully maintain Applicant's rights pursuant to 35 U.S.C. §135(b) as initially preserved in the parent application with respect to the above-identified patents issued to Kauffman and Ballivet. While the claims now presented for review are directed to generic aspects of the invention to facilitate examination of the application, these claims also comprehend specific aspects of the invention, for example as recited in the various dependent claims presented in the above-noted, First through Fifth Preliminary Amendments in the parent application, incorporated herein, that read on more detailed subject matter claimed in the foregoing Kaufmann and Ballivet patents. Accordingly, Applicants reserve the right to introduce additional claims directed to more detailed aspects of the invention, including additional claims relating directly back to claims presented by amendment in the parent application, during the course of the Office's review in this or a related application.

If for any reason the Examiner feels that a telephone conference would expedite prosecution of the subject application, the Examiner is invited to telephone the undersigned at (206) 467-9600.

Respectfully submitted,

Dated: August 28, 2000

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